

What is claimed is:

1. A method for identifying a subject at risk of breast cancer, which comprises detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the one or more polymorphic variations are detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c);

whereby the presence of the polymorphic variation is indicative of the subject being at risk of breast cancer.

2. The method of claim 1, which further comprises obtaining the nucleic acid sample from the subject.

3. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 133, 7938, 8873, 13221, 17288, 25732, 26923, 39977, 41284, 41410, 41477, 41514, 42606, 42742, 59515, 59808, 60265, 67152, 68332, 71128 and 76427.

4. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 7938, 26923, 39977 and 59808.

5. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 7938-59808 in SEQ ID NO: 1.

6. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 201, 6395, 8558, 9429, 9809, 10072, 10511, 11556, 16857, 16951, 17027, 17177, 17615, 17950, 18329, 18384, 18561, 18579, 18871, 27152, 27306, 28091, 28661, 29011, 29962, 29969, 30085, 31656, 31685, 31749, 45389, 45459,

46647, 49860, 53061, 57308, 61563, 61660, 62212, 67090, 67198, 70071, 70191, 74006, 75600, 85761, 90798, 90883, 91259, 95416, 95446, 96368, 97050, 97362, 97630, 97989 and 98107.

7. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 10511, 11556, 17177, 18384, 28661, 31656, 31685, 31749, 45389, 45459, 46647, 49860, 53061, 57308, 61563, 61660, 67090, 67198, 70071, 74006, 75600, 85761, 90798, 90883, 91259, 95416, 95446, 96368, 97362, 97630, 97989 and 98107.

8. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 10511-98107 in SEQ ID NO: 2.

9. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 160, 6053, 9719, 10481, 10676, 17179, 18561, 18658, 18694, 18858, 24582, 24683, 24767, 27402, 28150, 28494, 32003, 35588, 35619, 35856, 36254, 37314, 40033, 40095, 42593, 42799, 43090, 46683, 49774, 51796, 52079, 53857, 53971, 55899, 60682, 61291, 72720, 72752, 85507 and 89751.

10. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 160, 6053, 18658, 18694, 18858, 24683, 27402, 28494, 32003, 35588, 35856, 40095, 46683, 52079, 53857, 72720 and 72752.

11. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 160-72752 in SEQ ID NO: 3.

12. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 196, 13311, 14486, 14691, 15551, 17702, 17872, 19588, 19910, 20006, 20575, 21092, 22830, 23455, 23716, 23890, 24001, 24995, 27282, 27779, 29099, 31185, 33994, 34942, 35137, 36538, 37139, 37358, 38828, 39469, 40233, 40472, 41679, 41682, 42831, 42976, 44128, 44195, 46769, 47363, 48843, 52574, 52602, 53212, 53781, 54710, 55808, 57987, 58556, 59148, 59286, 60217, 60412, 60753, 60791, 61524, 62543, 62825, 62826, 62857, 63400, 63960, 64307, 64539, 65728, 66000, 66521, 68185, 69643, 74909, 82973, 83039, 85713, 86873, 90293, 91810, 92609, 92884 and 42831.

13. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 196, 13311, 14486, 19910, 20575, 23716, 23890, 24995, 29099, 33994, 34942, 37139, 40233, 40472, 42831, 42976, 44195, 48843, 58556, 59286, 60217, 62826, 62857, 63400, 63960 and 74909.

14. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in a region spanning positions 196-74909 in SEQ ID NO: 4.

15. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in linkage disequilibrium with one or more positions in claim 3, 6, 9 or 12.

16. The method of claim 1, wherein detecting the presence or absence of the one or more polymorphic variations comprises:

hybridizing an oligonucleotide to the nucleic acid sample, wherein the oligonucleotide is complementary to a nucleotide sequence in the nucleic acid and hybridizes to a region adjacent to the polymorphic variation;

extending the oligonucleotide in the presence of one or more nucleotides, yielding extension products; and

detecting the presence or absence of a polymorphic variation in the extension products.

17. The method of claim 1, wherein the subject is a human.

18. A method for identifying a polymorphic variation associated with breast cancer proximal to an incident polymorphic variation associated with breast cancer, which comprises:

identifying a polymorphic variation proximal to the incident polymorphic variation associated with breast cancer, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation;

determining the presence or absence of an association of the proximal polymorphic variant with breast cancer.

19. The method of claim 18, wherein the incident polymorphic variation is at a position in claim 3, 6, 9 or 12.

20. The method of claim 18, wherein the proximal polymorphic variation is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the incident polymorphic variation.

21. The method of claim 18, which further comprises determining whether the proximal polymorphic variation is in linkage disequilibrium with the incident polymorphic variation.

22. The method of claim 18, which further comprises identifying a second polymorphic variation proximal to the identified proximal polymorphic variation associated with breast cancer and determining if the second proximal polymorphic variation is associated with breast cancer.

23. The method of claim 22, wherein the second proximal polymorphic variant is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the proximal polymorphic variation associated with breast cancer.

24. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c); and
- (e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

wherein the nucleotide sequence comprises one or more polymorphic variants associated with breast cancer selected from the group consisting of a thymine at position 7938 in SEQ ID NO: 1, a cytosine at position 26923 in SEQ ID NO: 1, a thymine at position 39977 in SEQ ID NO: 1, a thymine at position 59808 in SEQ ID NO: 1, a thymine at position 10511 in SEQ ID NO: 2, a cytosine at position

11556 in SEQ ID NO: 2, a thymine at position 17177 in SEQ ID NO: 2, a thymine at position 18384 in SEQ ID NO: 2, an adenine at position 28661 in SEQ ID NO: 2, an adenine at position 31656 in SEQ ID NO: 2, an adenine at position 31685 in SEQ ID NO: 2, a guanine at position 31749 in SEQ ID NO: 2, a thymine at position 45389 in SEQ ID NO: 2, a guanine at position 45459 in SEQ ID NO: 2, an adenine at position 46647 in SEQ ID NO: 2, a thymine at position 49860 in SEQ ID NO: 2, a thymine at position 53061 in SEQ ID NO: 2, an adenine at position 57308 in SEQ ID NO: 2, a guanine at position 61563 in SEQ ID NO: 2, a guanine at position 61660 in SEQ ID NO: 2, a guanine at position 67090 in SEQ ID NO: 2, a cytosine at position 67198 in SEQ ID NO: 2, an adenine at position 70071 in SEQ ID NO: 2, a cytosine at position 74006 in SEQ ID NO: 2, an adenine at position 75600 in SEQ ID NO: 2, a guanine at position 85761 in SEQ ID NO: 2, a thymine at position 90798 in SEQ ID NO: 2, a cytosine at position 90883 in SEQ ID NO: 2, an adenine at position 91259 in SEQ ID NO: 2, a cytosine at position 95416 in SEQ ID NO: 2, a thymine at position 95446 in SEQ ID NO: 2, a thymine at position 96368 in SEQ ID NO: 2, a thymine at position 97362 in SEQ ID NO: 2, an adenine at position 97630 in SEQ ID NO: 2, a cytosine at position 97989 in SEQ ID NO: 2, a thymine at position 98107 in SEQ ID NO: 2, an adenine at position 160 in SEQ ID NO: 3, a guanine at position 6053 in SEQ ID NO: 3, a guanine at position 18658 in SEQ ID NO: 3, a guanine at position 18694 in SEQ ID NO: 3, a thymine at position 18858 in SEQ ID NO: 3, a guanine at position 24683 in SEQ ID NO: 3, a guanine at position 27402 in SEQ ID NO: 3, a thymine at position 28494 in SEQ ID NO: 3, an adenine at position 32003 in SEQ ID NO: 3, a cytosine at position 35588 in SEQ ID NO: 3, an adenine at position 35856 in SEQ ID NO: 3, a guanine at position 40095 in SEQ ID NO: 3, an adenine at position 46683 in SEQ ID NO: 3, an adenine at position 52079 in SEQ ID NO: 3, a cytosine at position 53857 in SEQ ID NO: 3, an adenine at position 72720 in SEQ ID NO: 3, a cytosine at position 72752 in SEQ ID NO: 3, an adenine at position 196 in SEQ ID NO: 4, a guanine at position 13311 in SEQ ID NO: 4, a thymine at position 14486 in SEQ ID NO: 4, a thymine at position 19910 in SEQ ID NO: 4, an adenine at position 20575 in SEQ ID NO: 4, a guanine at position 23716 in SEQ ID NO: 4, a guanine at position 23890 in SEQ ID NO: 4, an adenine at position 24995 in SEQ ID NO: 4, a cytosine at position 29099 in SEQ ID NO: 4, a thymine at position 33994 in SEQ ID NO: 4, a thymine at position 34942 in SEQ ID NO: 4, a thymine at position 37139 in SEQ ID NO: 4, a thymine at position 40233 in SEQ ID NO: 4, an adenine at position 40472 in SEQ ID NO: 4, a guanine at position 42831 in SEQ ID NO: 4, a guanine at position 42976 in SEQ ID NO: 4, a thymine at position 44195 in SEQ ID NO: 4, a thymine at position 48843 in SEQ ID NO: 4, an adenine at position 58556 in SEQ ID NO: 4, a guanine at position 59286 in SEQ ID NO: 4, an adenine at position 60217 in SEQ ID NO: 4, a cytosine at position 62826 in SEQ ID NO: 4, a thymine at position 62857 in SEQ ID NO: 4, a thymine at position 63400 in SEQ ID NO: 4, an adenine at position 63960 in SEQ ID NO: 4 and a cytosine at position 74909 in SEQ ID NO: 4.

25. An oligonucleotide comprising a nucleotide sequence complementary to a portion of the nucleotide sequence of (a), (b), (c), or (d) in claim 24, wherein the 3' end of the oligonucleotide is adjacent to a polymorphic variation associated with breast cancer.

26. A microarray comprising an isolated nucleic acid of claim 24 linked to a solid support.

27. An isolated polypeptide encoded by the isolated nucleic acid sequence of claim 24.

28. A method for identifying a candidate molecule that modulates cell proliferation, which comprises:

(a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:

(i) a nucleotide sequence in SEQ ID NO: 1-4;

(ii) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(iv) a fragment of a nucleotide sequence of (i), (ii), or (iii); or

introducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and

(b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,

whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate molecule that modulates cell proliferation.

29. The method of claim 28, wherein the system is an animal.

30. The method of claim 28, wherein the system is a cell.

31. The method of claim 28, wherein the nucleotide sequence comprises one or more polymorphic variations associated with breast cancer.

32. The method of claim 28, wherein the one or more polymorphic variations associated with breast cancer are at one or more positions in claim 3, 6, 9 or 12.

33. A method for treating breast cancer in a subject, which comprises administering a candidate molecule identified by the method of claim 28 to a subject in need thereof, whereby the candidate molecule treats breast cancer in the subject.

34. A method for identifying a candidate therapeutic for treating breast cancer, which comprises:

- (a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
 - (i) a nucleotide sequence in SEQ ID NO: 1-4;
 - (ii) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
 - (iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
 - (iv) a fragment of a nucleotide sequence of (i), (ii), or (iii); orintroducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and
- (b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,

whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate therapeutic for treating breast cancer.

35. The method of claim 34, wherein the test molecule inhibits cell proliferation or cell metastasis.

36. A method for treating breast cancer in a subject, which comprises contacting one or more cells of a subject in need thereof with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c); and

(e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

whereby contacting the one or more cells of the subject with the nucleic acid treats breast cancer in the subject.

37. The method of claim 36, wherein the nucleic acid is RNA or PNA.

38. The method of claim 37, wherein the nucleic acid is duplex RNA.

39. A method for treating breast cancer in a subject, which comprises: 7
detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the one or more polymorphic variation are detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-4;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

administering a breast cancer treatment to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

40. The method of claim 39, wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

41. The method of claim 39, wherein the breast cancer treatment comprises a nucleic acid comprising a nucleotide sequence complementary to a nucleotide sequence in SEQ ID NO: 1-4.

42. The method of claim 41, wherein the nucleic acid is a double stranded RNA.

43. The method of claim 39, which further comprises extracting and analyzing a tissue biopsy sample from the subject.

44. The method of claim 43, wherein the treatment is chemotherapy, surgery, radiation therapy, and combinations of the foregoing.

45. The method of claim 44, wherein the chemotherapy is selected from the group consisting of cyclophosphamide (Cytoxan), methotrexate (Amethopterin, Mexate, Folex), fluorouracil (Fluorouracil, 5-Fu, Adrucil), cyclophosphamide, doxorubicin (Adriamycin), and combinations of the foregoing.

46. The method of claim 45, wherein the combinations are selected from the group consisting of cyclophosphamide (Cytoxan), methotrexate (Amethopterin, Mexate, Folex), and fluorouracil (Fluorouracil, 5-Fu, Adrucil); cyclophosphamide, doxorubicin (Adriamycin), and fluorouracil; and doxorubicin and cyclophosphamide.

47. The method of claim 39, wherein the breast cancer treatment reduces breast cancer metastasis.

48. A method for detecting or preventing breast cancer in a subject, which comprises:
detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

administering a breast cancer prevention procedure or detection procedure to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

49. The method of claim 48, wherein the one or more polymorphic variations are detected at one or more positions in wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

50. The method of claim 48, wherein the breast cancer detection procedure is selected from the group consisting of a mammography, an early mammography program, a frequent mammography program, a biopsy procedure, a breast biopsy and biopsy from another tissue, a breast ultrasound and optionally ultrasound analysis of another tissue, breast magnetic resonance imaging (MRI) and optionally MRI analysis of another tissue, electrical impedance (T-scan) analysis of breast and optionally of another tissue, ductal lavage, nuclear medicine analysis (e.g., scintimammography), *BRCA1* and/or *BRCA2* sequence analysis results, thermal imaging of the breast and optionally of another tissue, and a combination of the foregoing.

51. The method of claim 48, wherein the breast cancer prevention procedure is selected from the group consisting of one or more selective hormone receptor modulators, one or more compositions that prevent production of hormones, one or more hormonal treatments, one or more biologic response modifiers, surgery, and drugs that delay or halt metastasis.

52. The method of claim 51, wherein the selective hormone receptor modulator is selected from the group consisting of tamoxifen, reloxifene, and toremifene; the composition that prevents production of hormones is an aromatase inhibitor selected from the group consisting of exemestane, letrozole, anastrozol, goserelin, and megestrol; the hormonal treatment is selected from the group consisting of goserelin acetate and fulvestrant; the biologic response modifier is an antibody that specifically binds herceptin/HER2; the surgery is selected from the group consisting of lumpectomy and mastectomy; and the drug that delays or halts metastasis is pamidronate disodium.

53. A method of targeting information for preventing or treating breast cancer to a subject in need thereof, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

directing information for preventing or treating breast cancer to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

54. The method of claim 53, wherein the one or more polymorphic variations are detected at one or more positions in wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

55. The method of claim 53, wherein the information comprises a description of a breast cancer detection procedure, a chemotherapeutic treatment, a surgical treatment, a radiation treatment, a preventative treatment of breast cancer, and combinations of the foregoing.

56. A method of selecting a subject that will respond to a treatment of breast cancer, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with breast cancer in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO: 1-4;
- (b) a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4 ;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-4 ; and
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

selecting a subject that will respond to the breast cancer treatment based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

57. The method of claim 56, wherein the one or more polymorphic variations are at one or more positions in wherein the one or more polymorphic variations are detected at one or more positions in claim 3, 6, 9 or 12.

58. A composition comprising a breast cancer cell and an antibody that specifically binds to a protein, polypeptide or peptide encoded by a nucleotide sequence identical to or 90% or more identical to a nucleotide sequence in SEQ ID NO: 1-8.

59. The composition of claim 58, wherein the antibody specifically binds to an epitope that comprises a glutamine at amino acid position 278 in SEQ ID NO: 9 or a glycine at amino acid position 389 in SEQ ID NO: 12.

//

60. A composition comprising a breast cancer cell and a RNA, DNA, PNA or ribozyme molecule comprising a nucleotide sequence identical to or 90% or more identical to a portion of a nucleotide sequence in SEQ ID NO: 1-8.

61. The composition of claim 60, wherein the RNA molecule is a short inhibitory RNA molecule.